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EXAMINER	
KHANNA, HEMANT	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,239	TARASOVA ET AL.	
	Examiner	Art Unit	
	Hemant Khanna	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,49-64,67-71,76-81 and 86-119* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,14-18,20,28,49-52,54,62,64,67,88,90,98,99,101,110 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/19/04, 01/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,7-13,19,21-27,53,55-61,68-71,76-81,86,87,89,91-97,100,102-109 and 112-119.

DETAILED ACTION

1. Applicant's election with traverse of claims 1-4, 6, 14-18, 20, 28, 49-52, 54, 62-64, 67, 88, 90, 98, 99, 101, 110, and 111 that belong to the invention of SEQ ID NO: 20 from the Group of inventions (1-15) in the reply filed on February 12, 2007 is acknowledged. The traversal is on the ground(s) that the claims of Groups (1-90) are all linked by the technical feature of a conjugate comprising a ligand, and a cytotoxic agent linked by a linking molecule (Remarks, page 4, paragraph 4). Further, the Applicants argue that certain subgroups of claims have other special technical features such as sharing a ligand bound to a cytotoxic agent by a linking molecule of FALA (SEQ ID NO:1), and the recitation of specific ligands and cytotoxic agents does not change the nature of the claims as sharing the above special technical feature (Remarks, page 4, paragraph 5). Hence, the pending claims and species should be examined together in this application.

The applicant's arguments are not found persuasive. The Group of inventions (1-15) do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group of inventions (1-15) are drawn to sequences represented by SEQ ID NO: 5-18, and 20. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical feature as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of similar nature. See MPEP 1850 (III)B. However, the Group of inventions (1-15) recite alternatives that do not

share a common property or common structure. Hence, the requirement for a same and corresponding special technical feature as defined in PCT Rule 13.2 is lacking.

Additionally, the Group of inventions (16-90) do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group of inventions (16-90) are drawn to linkers with non-overlapping sequences represented conjugated to SEQ ID NO: 5-18, and 20, which are not alternatives of similar nature as discussed above. Further, the shared technical feature of the Group of inventions represented by the conjugate comprising a linker ALALA, linking a cytotoxic agent and a ligand that binds to CCKB receptor is rendered obvious by Czerwinski (PNAS, 1998 95:11520-11525, cited by the Applicant in the IDS filed 08/19/04), and hence is not a contribution over the prior art.

The restriction between Group of inventions (1-90) is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's species of the linker FALA conjugated to the invention of SEQ ID NO:20 is free of the prior art. Applicant's species of FALA conjugated to the invention of SEQ ID NO:20 reads on claims 1-4, 6, 14, and 63.

For the benefit of the Applicant, the Examiner extended the search to other species of linkers conjugated to the invention of SEQ ID NO:20, which were also found free of the art. Other species of linkers conjugated to the invention of SEQ ID NO:20 read on claims 15-18, 20, 28, 49-52, 54, 62, 64, 67, 88, 90, 98, 99, 101, 110, 111.

The Examiner then extended the search to the generic claims which stand rejected under 35 USC 102(b) and 35 USC 112, first paragraph as set forth below.

Claims 5, 7-13, 19, 21-27, 53, 55-61, 68-71, 76-81, 86-87, 89, 91-97, 100, 102-109, 112-119 are withdrawn from consideration as being drawn to a non-elected invention. Election was made **with** traverse in the reply filed on February 12, 2007.

Specification

2. The disclosure is objected to because of the following informalities: the sequence FLALAEEEAYGW(Nle)DF on page 13, paragraph [0042] has a typographical error in the linker sequence represented by FLALA. It is the Applicant's intention to represent the linker as FALA. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4, 6, 14-18, 20, 28, 49-52, 54, 62-64, 67, 88, 90, 98, 99, 101, 110, and 111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co. the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In Gostelli, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) level of skill and knowledge in the art, (2) partial structure, (3) physical and/or chemical properties, (4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) method of making the claimed invention.

In the instant case, the claims are drawn to a conjugate comprising a ligand, linker, and a cytotoxic agent, in which the linker is FALA, VLALA, ChaLALA, ChaChaLAL, NAlChaLAL, NalLALA, ALAL, and ALALA.

(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to preparation of conjugates comprising ligand, linker, cytotoxic agent and determination of the binding behavior of the conjugate to the CCKB receptor.

(2) Partial structure:

N-terminal truncated derivatives of gastrin-34 (ligand) whose representatives do not share a common structure of sequence. No common structure among cytotoxic agents. No structures of derivatives disclosed. No common sequence among linkers disclosed.

(3) Physical and/or chemical properties:

Agents ligated to peptides are cytotoxic

(4) Functional characteristics:

No agonist or antagonist properties recited, with the exception of binding properties of ligands to CCKB receptor

(5) Method of making the claimed invention:

Standard solid-phase and solution phase synthesis of making peptide ligands and conjugating cytotoxic agents and linkers

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claims 1, 15, 49, 88, and 99 are broad generics, with respect to all possible ligands, and cytotoxic agents encompassed by the claims. The possible structural variations are limitless to the class of ligands to CCKB and cytotoxic agents conjugated to the ligands. It must not be forgotten that the MPEP states that if a

biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. "MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between the function of binding to CCKB and structure of all ligands, and all recited linkers beyond the ligands, linkers and cytotoxic agents disclosed in the examples in the specification.

The specification describes SEQ ID NO:20 conjugated to cytotoxic agent hemiasterlin or cemadotin via the linker VLALA but the examples do not demonstrate the conjugation of cemadotin to FALA or describe the structures of the derivatives thereof that demonstrate the binding to CCKB.

While the specification describes SEQ ID NO:20 conjugated to cytotoxic agent cemadotin via the linker VLALA, there is insufficient description to accept that the cytotoxic agents linked via other linkers would bind to CCKB.

While having written description for truncated gastrin peptides identified in the specification, the specification is void of any ligands with functional characteristics that qualify the ligands being binders of all recited receptors, with the exception of CCKB. There is insufficient description of any and all sequences of other peptides of the gastrin with the exception of the sequence of SEQ ID NO:20 that would allow one of skill in the art to practice the invention as claimed. The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might

achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 99, and 101 are rejected under 35 U.S.C. 102(b) as being anticipated by Czerwinski (PNAS, 1998 95:11520-11525, cited by the Applicant in the IDS filed 08/19/04).

The instant claims are drawn to a conjugate, and a composition with a carrier, further comprising a ligand, a linker, and a cytotoxic agent, in which the linker is ALALA, and wherein the ligand specifically binds to a receptor selected from CCKB receptor.

Czerwinski disclose EAG (Materials and Methods, page 11521) as the conjugate comprising the linker ALALA, a ligand, and a cytotoxic agent (EII) to define the structural requirements for the CCKB receptor (right column, paragraph 2, page 11520; left column, paragraph 2, page 11522), thus meeting the limitations of claim 99.

With respect to claim 101, and to the extent that the Applicant defines a carrier as any used conventionally, and whose use is limited only by chemico-physical

considerations, such as solubility and lack of reactivity with the conjugates of the present invention, the carrier of Czerwinski (DMSO) is deemed to have sufficient similarity to the carrier of the instant Applicant to shift the burden to the Applicant to provide evidence that the claimed carrier is unobviously different from the carrier of Czerwinski.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

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Hemant Khanna Ph.D.
April 25, 2007

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